

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>5</sup> :</b> <b>A01N 65/00, A61K 35/78, 7/16</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 94/09631</b> <b>(43) International Publication Date:</b> 11 May 1994 (11.05.94)
<b>(21) International Application Number:</b> PCT/EP93/02997 <b>(22) International Filing Date:</b> 28 October 1993 (28.10.93) <b>(30) Priority data:</b> 9222985.5 3 November 1992 (03.11.92) GB <b>(71) Applicant (for all designated States except US):</b> GISQUARE TECHNOLOGIES B.V. [NL/NL]; Museumplein 11, NL-1071 DJ Amsterdam (NL). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only) :</b> ROVESTI, Guido [IT/IT]; Via Degli Arcimbaldi, 2, I-20123 Milano (IT). SE-GALLA, Gabriele [IT/IT]; Via Milano, 70, I-34019 Peschiera del Garda (IT). LA FRATTA, Pietro [IT/IT]; Via Cesariano, 6, I-20154 Milano (IT). DI SCHIENA, Michele, Giuseppe [IT/IT]; Via Garibaldi, 17, I-20080 Cislano (IT).		<b>(74) Agent:</b> BIANCHETTI, Giuseppe; Studio Consulenza Brevettuale, Via Rossini, 8, I-20122 Milano (IT). <b>(81) Designated States:</b> AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> USE OF THE TARCHONANTHUS CAMPHORATUS  <b>(57) Abstract</b>  Use of Tarchonanthus camphoratus parts and its derivatives in insect-repelling, anti-irritating, soothing, anti-œdema, decongesting formulations and compositions.		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

USE OF THE TARCHONANTHUS CAMPHORATUS

This invention is referred to new uses of the *Tarchonanthus camphoratus*, utilization of its leaves, roots and branches either fresh, dried, soaked, extracted or in the form of essential oil.

5       The *Tarchonanthus camphoratus* is a shrub rearing in the wild in different African regions especially in the Rift uplands area. An experimental growing took also place in Italy (Canzonieri and Spica; Gazz. Chim. Ital. 1882, 227).

10       The shrub, mostly unknown by botanists, has different names such as: Wild cotton, Sage wood, Wildesalie, Kamferhout, Kamferbos, Sieriehout, Vaalbos, Veld-vaalbos, Vaaibos, Sauto Mofahlana, Rolog e Thaalaping mohathla, well known in the local Swahili  
15       dialect with the name of "Leleshua", in the abissianian language "Ebok" and so on, or simply with the botanic name of *Tarchonanthus camphoratus*.

20       The *Tarchonanthus camphoratus* is a shrub reaching 2-4 m height; belonging to the Composite family, it has regular branches with velutinous white-greenish oval or lanceolate shaped leaves ranging from 4 to 13 cm lenght having a strong camphorated aromatic smell, whence its Linneana denomination.

25       This plant, with its wool-like, spike shaped flower heads is mentioned only in "The Medicinal and Poisonous Plants of Southern Africa" by John Mitchell Watt and Maria Gerdina Breyer-Brandwijk - Edimburgh, 1932 and in Paolo Rovesti's communication, presented at the XXIX International Congress of Industrial Chemistry

in Paris in December 1956, "Ecological influences on the composition of the essential oils".

In the literature, mentioned herewith, various applications of this plant are known.

- 5     - Engler mentions this species as used only for wood by the Usambara in Tanzania (Die Pflanzenwelt Afrikas - Teil B. Berlin, 1895, 357).
- Braun tells the Masai (Tanzania) use it for wood-carving (Neil Gew. Pfl. Bd. XI, 2, 47).
- 10    - Thonner is generally speaking about the plant precious medicinal properties using its leaves in fumigations and infusions (Die Blütenpflanzen Afrikas - Berlin 1908).
- Dragerdorff tells that this species have the same  
15       therapeutic applications as *Salvia officinalis* (sage) (Die Heilpflanzen - Stuttgart 1898, 589).
- Canzonieri and Spica made some studies about the supposed antipyretic properties/activities of  
20       *Tarchonantus Camphoratus* leaves (Gazz. Chim. Ital. 1882, 227).
- Watt and Breyer tell the Ottentotti and other indigenous in the South Africa smoke the plant leaves using it as tobacco thanks to their slight  
25       narcosis forms. They are also used in fumigations against headache, rheumatism and infusions (The medicinal and poisonous Plants of South Africa -  
Edimburg - 1932, 189) against dyspepsia and tooth-ache.- Pappe tells leaves contain some camphor but he gives no practical proof (Florae Capensis  
30       Medicae Prodrumus - Capetown - 1868, 178).
- Pijper distilled an essential oil but he gave no

details on its characteristics (De Volksgeneskunst in Transvaal - Leyden, 1919).

- 5                   - De Stefanis distilled, using some small branches with leaves sent from Eritrea to the Farmacognosia Laboratory of Turin University, an essence having a strong camphorated smell, with a yield of 0.1% and the following peculiarity:

10                   D 0,9152; i.a. 2,1; i.s. 11,8; i.s. after acetylene 85; I. Iodine 188,5; solubility 1:0.5 in alcohol at 95° (Boll. Inf. Econ. Minist. Colonie - Roma, 1924, n. 1).

- 15                   - Further details come from Rovesti's documentation which shows two plant distillations made in February (dried season) and in August (damp season) which took place in the Ethiopian tableland (XXIX International Congress of Industrial Chemistry, above cited).

	Yield%	$d_{15}^{\circ}$	$D_{20}^{\circ}$	$n_D^{20}$	I.S.	I.S. after acethyl.	Sol.
February essence	0.108	0.9171	-7°23'	1.4681	31.73	149.33	1:3A 70°
August essence	0.209	0.8968	-2°15'	1.4718	18.67	41.07	1:3A 90°

It has now been found, and this is the subject of this invention, that some parts of the plant, in particular its leaves, fresh or dried and their derivatives, have some special insect repelling, insecticide, anti-oedema, decongestant, anti-irritating and smoothing properties that might be profitably used for therapeutic applications both for humans and animals.

The derivatives of this invention concern the *Tarchonanthus camphoratus* extracts obtained through an extraction as mentioned for example in the Italian Pharmacopeia.

Few examples of extraction methods are: maceration, decoction, percolation and distillation.

There are then different derivatives such as the aqueous, the glycolic, the alcoholic, the hydroalcoholic, the soft and dried ones and, preferably, the essential oils.

One of the main goals of this invention is the use of the essential oil. According to the present invention, the application of this plant and of their derivatives concerns not only its insect repelling and insecticide action but also the treatment of irritations and inflammations caused by insect bites.

The efficacy of the *Tarchonanthus camphoratus* derivatives has been also found during some irritation and inflammatory conditions on cutis as for example eczema, acne, reddening, swelling and on genital and mouth mucosa.

The *Tarchonanthus Camphoratus* essential oil obtained through a distillation in a steam flow, has

been characterized using a GC/MS analysis, in this way 44 components were identified. Among these elements we find:

	Alpha Pinene	15.40%
5	Camphene	4.35%
	Beta Pinene	3.50%
	Delta-2-Carene	4.30%
	Alpha Phellandrene	1.60%
	Limonene	3.00%
10	Gamma Terpinene	2.05%
	Terpinolene	1.35%
	1,8 Cineole	12.10%
	Fenchol	14.40%
	1-Terpinen-4-ol	2.30%
15	Alpha Terpineol	4.50%
	Fenchone	0.85%
	Trans Caryiophyllene	1.15%
	Bergamotene	4.50%
	Delta Cadinene	1.40%
20	Alpha Curcumene	1.70%

The results of this research were presented at the Digne Congress in September 1992 (Ghizzoni, Rovesti, Colombo, Bottini).

Basing on a test of primary cutis irritation on human, it appears that the *Tarchonanthus camphoratus* oil spreaded as it is on 20 volunteers' healthy cutis in occlusive conditions, gave a medium irritation index of 0.4 after 15 minutes and of 0.35 after 24 hours the sample removal. Basing on the above mentioned parameter the product is then classified as non irritating.

The essential oil showed some surprising

therapeutic anti-oedema properties. The information about the applications of the essential oil, concerns in detail the oedema status on lower limbs.

Another object of the present invention are the  
5 topical pharmaceutical compositions containing from 0.01 to 10% of *Tarchonanthus camphoratus* essential oil used as an active ingredient, alone or combined with other active materials.

The compositions can be made according to  
10 conventional methods as reported, for example, in the "Remington's Pharmaceutical Sciences Handbook" Mack Pub. N.Y. U.S.A.

Some examples of pharmaceutical topical  
compositions are: solutions, suspensions, emulsions,  
15 ointments, creams, toothpastes in gel form, sprays, prolonged release compositions such as transdermic plasters, and soaps.

One of the preferred embodiments of this invention is the preparation of insect-repelling and insecticide  
20 formulations containing from 0.01 to 10% of *Tarchonanthus camphoratus* essential oil as active ingredient, alone or with other similar components having the same activity.

Some examples of these preparations are: mosquito-  
25 fumigants, fumigants, vaporizing solutions, plates, sprays, stick, lotions, creams and gels.

The *Tarchonanthus* essential oil, put in different topical compositions having anti-oedema, decongestant, anti-irritating, soothing activity, can be used in  
30 quantities ranging from 0.01% to 5%, preferably from 0.03% to 0.5%.

On the other side the Tarchonanthus essential oil, put in different topical formulations with insect-repelling and insecticide activity, can be used in quantities ranging from 0.03% to 7%, preferably from 0.05% to 3%.

In insect-repelling formulations, where the shrub or its essential oil are used at their natural state, the quantity must be 5% up to 95%. In this case it is advisable to use the plant during its balsamic period and immediately after its picking up; this, unfortunately, sets a limit to the Tharconanthus use at natural state, while no limit is fixed for its essential oil.

The activity of the essential oil, being part of this invention, has been tested in more than one pharmacological and clinical test.

1. Insect-repelling and insecticide activity.

A spray lotion containing 0.05% Tarchonanthus essential oil, in respect to the below mentioned formulation in example n. 1, was spreaded on 10 volunteers' skin who, during summer season evenings, laied in places with a high mosquitoes concentration.

It has been showed that among the 10 volunteers only 2 of them had mosquito-bites on two cutis areas.

A spray lotion containing 3% Tarchonantus essential oil, in respect to the below mentioned formulation in example n. 3, was spreaded on 10 volunteers' skin who laied in places with a high mosquitoes concentration during summer evenings. It was showed that none of them had bites on the skin.

A Tarchonantus camphoratus essential oil alcoholic

lotion, in respect to the below mentioned formulation in example n. 4, was used in a diffusor with absorbant tampon and put in a dimly airy room of about 60 mc infested with bothersome insects. Once the diffuser worked, an insecticide action started.

2. Anti-oedema, decongestant, anti-irritating and soothing activity.

An application of 0.1% Tarchonanthus essential oil gel, as per formulation in example 5, was spreaded on oedematous legs, which gave immediate relief.

A gel containing 0.05% Tarchonatus essential oil, as per formulation in example 6, was put on female genitals with itching problems. That brought an immediate relief.

A gel containing 0.05% Tarchonanthus essential oil was used as per formulation in example 5, against bags under one's eyes. A rapid and surprising recovery took place.

A gel on 0.3% Tarchonantus essential oil basis, as mentioned in example n. 9, was used on a right ear as a remedy for a swelling due to a mosquito, or some other unidentified insect-bite. The problem was immediately solved. The same result was obtained after an application on different skin areas on 10 persons with various insect bites.

A gel on 0.05% Tarchonantus essential oil basis, as mentioned in example n. 6, was spreaded on 10 persons suffering from frequent erythema generally treated with a cortisone cream. It was found that all the subject recovered rapidly and both the painful and itching sensations disappeared.

An alcoholic solution containing 0.1% Tarchonantus essential oil, see example n. 12, was put, by means of a tampon, on a pimply skin full with acne on 10 patients. In all the above metioned situations the  
5 problem was totally solved. The same preparation was put on recent pimples that disappeared 24 hours later.

A gel with 0.1% Tarconanthus essential oil was used, as per example n. 7, on 5 subjects' face and neck skin and on armpits and legs suffering from irritation  
10 after shaving and depilation treatments. They both declared a relief and freshness sensation.

A fluid emulsion containing 0.1% Tarchonanthus essential oil, as per example n.13, was spreaded on genital and anal areas on 2 aged people and on 3 new  
15 borns, suffering from itching conditions due to napkins use. All the cases were solved rapidly.

A fluid emulsion on 0.1% Tarchonantus essential oil, see example 14, was spreaded on bedsores on 3 patients. In all these cases the recovery was rapid,  
20 the oedema and the irritation improved.

A gel containing 0.5% Tarchonantus essential oil, as per example n. 6, was spreaded on 7 subject with itching problems on the anal area due to emorrhoids and  
25 rhagades. They recovered rapidly declaring a freshness and relief sensation.

A mouthwash with 20% infusion, worked at cold state, obtained from Tarchonantus grinded fresh leaves, as in example n.16, was used on 5 patients having  
30 irritated gums. In these cases a constant and periodic application brought a relief with a consequent decongestion of gums together with a freshness

sensation and a good smelling breath.

A toothpaste with 0.2% Tarchonanthus essential oil, as mentioned in example n. 15, was used in 5 cases suffering from slightly irritated gums. A constant and periodic use of the formulation was of help in the gums decongestion. A freshness sensation and a good smelling breath was also noticed.

An alcoholic gel containing 1% Tarchonanthus essential oil, as per example n. 10, was used on legs suffering from phlebitis. A constant and periodic use was of help to solve the problem.

An alcoholic gel containing 0.8% Tarchonanthus essential oil as per example n. 11, was spreaded on haematoma on 3 subjects. In both cases, a constant and periodic use, was of help to improve the oedema problem.

The following examples further illustrate the invention. For sake of brevity, the essential oil is called E.O.

#### 20 **EXAMPLE N. 1**

##### Insecticide spray lotion

PEG 40 Hydrogenated Castor Oil	0.2	%
Glycerine	3	%
Tarchonanthus camphoratus E.O.	0.05	%
25 Preservatives (antibacterial/antimould)	q.s.	
Demineralized water	q.s. to 100%	

#### **EXAMPLE N. 2**

##### Insecticide spray lotion

PEG 40 Hydrogenated Castor oil	4	%
30 Glycerine	3	%
Tarchonanthus camphoratus E.O.	1	%

Preservatives (antibacterial/antimould)	q.s.
Demineralized water	q.s. to 100%

**EXAMPLE N. 3**Insecticide spray lotion

5	Peg 40 Hydrogenated Castor Oil	12	%
	Glycerine	3	%
	Tarchonanthus camphoratus E.O.	3	%
	Preservatives (antibacterial/antimould)	q.s.	
	Demineralized water	q.s. to 100%	

10 **EXAMPLE N. 4**Insecticide alcoholic solutions for environmental purposes

	Methylated alcohol type A	42	%
	Tarchonanthus camphoratus E.O.	5	%
15	Sorbitan monoleate 20 (OE)	13	%
	Demineralized water	q.s. to 100%	

**EXAMPLE N. 5**Ante-oedema gel

	Carboxyvinyl polymer (Carbomer 940)	0.76	%
20	Glycerine	3	%
	Sorbitan 20 (OE) monolaurate	0.4	%
	Tarchonanthus camphoratus E.O.	0.1	%
	Preservatives (antibacterial/antimould)	q.s.	
	Triethanolamine	0.5	%
25	Demineralized water	q.s. to 100%	

**EXAMPLE N. 6**Anti-irritating, soothing gel

	Carboxyvinyl polymer (Carbomer 940)	0.76	%
	Glycerine	3	%
30	Sorbitan 20 (OE) monolaurate	0.2	%
	Tarchonanthus camphoratus E.O.	0.05	%

Preservatives (antibacterial/antimould)	q.s.	
Triethanolamine	0.5	%
Demineralized water	q.s. to 100%	

**EXAMPLE N. 7**5 Anti-irritating gel pre/after shave/depilation

Carboxyvinyl polymer (Carbomer 940)	0.5	%
Glycerine	3	%
Sorbitan 20 (E.O.) monolaurate	0.2	%
Tarchonanthus camphoratus E.O.	0.04	%

10 Preservatives (antibacterial/antimould)	q.s.	
Triethanolamine	0.3	%
Demineralized water	q.s. to 100%	

**EXAMPLE N. 8**After sun gel

15 Carboxyvinyl polymer (Carbomer 940)	0.76	%
Glycerine	3	%
Sorbitan 20 (OE) monolaurate	0.4	%
Tarchonanthus camphoratus E.O.	0.1	%
Preservatives (antibacterial/antimould)	q.s.	
20 Triethanolamine	0.5	%
Demineralized water	q.s. to 100%	

**EXAMPLE N. 9**Anti-oedema gel

25 Carboxyvinyl Polymer (Carbomer 940)	0.70	%
Glycerine	3	%
Sorbitan 20 (OE) monolaurate	1.2	%
Tarchonanthus camphoratus E.O.	0.3	%
Preservatives (antibacterial/antimould)	q.s.	
Triethanolamine	0.45	%
30 Demineralized water	q.s. to 100%	

**EXAMPLE N. 10**Anti-oedema alcoholic gel

	Carboxyvinyl polymer (Carbomer 940)	0.5	%
	Alcohol type D	40	%
5	Glycerine	5	%
	Peg 40 Hydrogenated Castor Oil	3	%
	Tarchonanthus camphoratus E.O.	1	%
	Preservatives (antibacterial/antimould)	q.s.	
	Triethanolamine	0.3	%
10	Demineralized water	q.s. to 100%	

**EXAMPLE N. 11**Soothing/refreshing alcoholic gel

	Carboxyvinyl polymer (Carbomer 940)	0.5	%
	Alcohol type D	40	%
15	Glycerine	5	%
	Peg 40 Hydrogenated Castor Oil	2.5	%
	Tarchonanthus camphoratus E.O.	0.8	%
	Preservatives (antibacterial/antimould)	q.s.	
	Triethanolamine	0.3	%
20	Demineralized water	q.s. to 100%	

**EXAMPLE N. 12**Alcoholic solution for pimply skins

	Alcohol type C	40	%
	Glycerine	2	%
25	Sorbitan 20 (OE) monolaurate	2	%
	Tarchonanthus camphoratus E.O.	0.1	%
	Lavender e.o.	0.4	%
	Demineralized water	q.s. to 100%	

**EXAMPLE N. 13**Anti-irritating fluid emulsion

	Carboxyvinyl polymer (Carbomer 940)	0.30	%
	Glycerine	6	%
5	Tarchonanthus camphoratus E.O.	0.1	%
	Triethanolamine	0.2	%
	Acetylated Lanoline	1	%
	Dimethylpolyxyloxane	1	%
	Myristil lactate	2	%
10	Decyle oleate	2	%
	Preservatives (antibacterial/antimould)	q.s.	
	Demineralized water	q.s. to 100%	

**EXAMPLE N. 14**Anti-irritating/decongestant fluid emulsion

15	Carboxyvinyl plymer (Carbomer 940)	0.30	%
	Glycerine	6	%
	Tarchonanthus camphoratus E.O.	0.1	%
	Allantoine	1	%
	Tocopheryl acetate	0.5	%
20	Triethanolamine	0.2	%
	Acetylated lanoline	1	%
	Dimethylpolyxiloxane	1	%
	Myristil lactate	2	%
	Decyl oleate	2	%
25	Preservatives (antibacterial/antimould)	q.s.	
	Demineralized water	q.s. to 100%	

**EXAMPLE N. 15**Gum toothpaste

	Potassium sorbate	0.2	%
30	Glycerine	11	%
	Sorbitan 20 (OE) monolaurate	0.8	%

	Tarchonanthus camphoratus E.O.	0.2	%
	Carboxyvinyl cellulose medium density	1.5	%
	Dicalcium phosphate di-hydrate	48	%
	Sorbitol 70%	11	%
5	Sodium laurylether sulphate	2	%
	Acesulfame Hoechst (sweetener)	0.2	%
	Preservatives (antibacterial/antimould)	q.s.	
	Demineralized water	q.s. to 100%	

**EXAMPLE N. 16**10 Idroalcoholic mouthwash

	Alcohol type E	15	%
	Glycerine	4	%
	Glycyrrhizinate ammonium	0.1	%

15	Tarchonanthus infusion at cold state grinded fresh leaves at slow stirring for 7 days in demin. water preserved	20	%
	Demineralized water	q.s. to 100%	

**EXAMPLE N. 17**Mosquito fumigant

20 A convenient quantity of dried leaves, belonging to a plant picked up by no more than 30 days, was grinded small.

30% of it was mixed up with arabic gum (10%), pit-coal (50%) potassium nitrate (10%), worked in water, spiral  
25 shaped and dried in a heater at 35°C for 24 hrs.

The same examples can be formulated with extracts and soaked in the proper concentrations.

CLAIMS

1. The use of *Tarchonanthus camphoratus* parts or a derivative thereof as insect-repelling, anti-irritating, soothing, anti-oedema, or decongesting agent.  
5
2. The use of *Tarchonanthus camphoratus* extracts as an insect-repelling, anti-irritating, soothing, anti-oedema, or decongesting agent.
- 10 3. The use of *Tarchonanthus camphoratus* essential oil as insect-repelling, anti-irritating, soothing, anti-oedema, or decongesting agent.
4. A topical pharmaceutical composition containing *Tarchonanthus camphoratus* as active ingredient.
- 15 5. A topical pharmaceutical composition containing *Tarchonanthus camphoratus* parts, derivative, extract or essential oil as active ingredient in a concentration of 0.05 to 10%.
6. The use of *Tarchonanthus camphoratus* parts, or a derivative thereof in the preparation of an insect-repelling or insecticide formulation.  
20
7. The use of *Tarchonanthus camphoratus* extract in the preparation of an insect-repelling or insecticide formulation.
- 25 8. The use of *Tarchonanthus camphoratus* essential oil in the preparation of an insect-repelling or insecticide formulation.
9. An insect-repelling or insecticide formulation containing 5% to 95% of *Tarchonanthus camphoratus* parts, derivative, extract or essential oil.  
30

## INTERNATIONAL SEARCH REPORT

Internat. Application No

PCT/EP 93/02997

## A. CLASSIFICATION OF SUBJECT MATTER

A 01 N 65/00, A 61 K 35/78, A 61 K 7/16

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A 01 N, A 61 K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LA GAZZETTA CHIMICA <sup>1</sup> ITALIANA, An. XII, vol. XII, 1982, Palermo F. CANZONERI et al. "Ricerche sui Tarchonanthus Canphora- tus", pages 227-31, the whole document.	1-9
A	CHEMICAL ABSTRACTS, vol. 91, no. 25, issued 17 October 1979 (Columbus, Ohio, USA), F. BOHLMAN et al. "Naturally occurring terpene derivati- ves. Part 189. A new bisa- bolene derivative and a new dihydrocaffeic acid deriva- tive from Tarchonanthus trilobus."	1-9

☐ Further documents are listed in the continuation of box C.☐ Patent family members are listed in annex.

## \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

03 February 1994

Date of mailing of the international search report

01.03.94

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

SCHNASS e.h.

## INTERNATIONAL SEARCH REPORT

-2-

Intern

Application No

PCT/EP 93/02997

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>page 704, abstract no. 211594p &amp; Phytochemistry 1979, 18(4), 677-8.</p> <p>--</p> <p>DERWENT ACCESSION No. 66-33 730, Questel Telesystems (WPIL), DERWENT PUBLICATIONS LTD., London, abstract &amp; ZA 6704243 (WILMANS JJ).</p> <p>----</p>	1-9

**THIS PAGE BLANK (USPTO)**